

fluorinated gas, [in combination with] and bearing a targeting ligand, wherein said targeting ligand is covalently bound to said lipid vesicles via a hydrophilic polymer linking group, said targeting ligand targets cells or receptors selected from the group consisting of myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIbIIIa receptor and said fluorinated gas is selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

Cancel Claim 101, without prejudice.

102. (Amended) A formulation according to Claim [101] 100 wherein said lipid vesicles are selected from the group consisting of micelles and liposomes.

113. (Amended) A process for the preparation of a formulation for diagnostic or therapeutic use which comprises, in combination with a bioactive agent, lipid[, polymer or protein] vesicles encapsulating a fluorinated gas, in combination with a targeting ligand, wherein the process comprises combining together said bioactive agent, lipid, [protein or polymer,] fluorinated gas and targeting ligand, wherein said targeting ligand [targets cells or receptors selected from the group consisting of myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIbIIIa receptor] comprises the sequence Lys-Gln-Ala-Gly-Asp-Val (SEQ ID NO 1), and said fluorinated gas is selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

Cancel Claim 114, without prejudice.

115. (Amended) A process according to Claim [114] 113 wherein said [lipids] lipid vesicles are selected from the group consisting of liposomes and micelles.

122. (Amended) A targeted formulation for diagnostic or therapeutic use comprising, in combination with a bioactive agent, lipid[, polymer or protein] vesicles encapsulating a fluorinated gas, in combination with a targeting ligand, wherein the formulation is prepared by a process which comprises combining together said bioactive agent, lipid, [protein or polymer,] fluorinated gas and targeting ligand, wherein said targeting ligand [targets cells or receptors selected from the group consisting of myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIbIIIa receptor] comprises the sequence Lys-Gln-Ala-Gly-Asp-Val (SEQ ID NO 1), and said fluorinated gas is selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

Cancel Claim 123, without prejudice.

124. (Amended) A targeted formulation according to Claim [123] 122 wherein said lipid vesicles are selected from the group consisting of liposomes and micelles.

127. (Amended) A method for the therapeutic delivery *in vivo* of a bioactive agent comprising administering to a patient a therapeutically effective amount of a formulation which comprises, in combination with a bioactive agent, lipid[, protein or polymer] vesicles encapsulating a fluorinated gas, [in combination with] and bearing a targeting ligand, wherein said targeting ligand is covalently bound to said lipid vesicles via a hydrophilic polymer linking

group, said targeting ligand targets cells or receptors selected from the group consisting of myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIbIIIa receptor and said fluorinated gas is selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

194. (Amended) A formulation according to Claim [101] 100 wherein said lipid vesicles comprise a phospholipid.

Cancel Claims 201 and 202, without prejudice.

203. (Amended) A formulation according to Claim [202] 100 wherein said hydrophilic polymer comprises polyethylene glycol.

Cancel Claims 204 to 209, without prejudice.

229. (Amended) A process according to Claim [114] 113 wherein said lipid vesicles comprise a phospholipid.

236. (Amended) A process according to Claim [114] 113 wherein said lipid vesicles further comprise a polymer.

Cancel Claims 239 to 244 and 249 to 254 , without prejudice.

261. (Amended) A targeted formulation according to Claim [123] 122 wherein said lipid[vesicles comprise] comprises a phospholipid.

262. A targeted formulation according to Claim 261 wherein said phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine and phosphatidic acid.

268. (Amended) A targeted formulation according to Claim [123] 122 wherein said lipid vesicles further comprise a polymer.

Cancel Claims 271 to 276, 281 to 286 and 293, without prejudice.

294. (Amended) A method according to Claim [293] 127, wherein said lipid vesicles comprise a phospholipid.

Cancel Claims 301 and 302, without prejudice.

303. (Amended) A method according to Claim [302] 127 wherein said hydrophilic polymer comprises polyethylene glycol.

Cancel Claims 304 to 309 and 330, without prejudice.

331. (Amended) A method according to Claim [330] 329, wherein said lipid vesicles comprise a phospholipid.

Cancel Claims 338 to 346, without prejudice.

351. (Amended) A method according to Claim 329 wherein said targeting ligand comprises [the] a sequence selected from the group consisting of Arg-Gly-Asp and Lys-Gln-Ala-Gly-Asp-Val (SEQ ID NO 1).

Please add the following claims:

--357. A targeted formulation for therapeutic or diagnostic use comprising, in combination with a bioactive agent, lipid vesicles encapsulating a fluorinated gas, in combination with a targeting ligand, wherein said targeting ligand comprises the sequence Lys-Gln-Ala-Gly-Asp-Val (SEQ ID NO 1), and said fluorinated gas is selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

358. A targeted formulation according to Claim 357 wherein said lipid vesicles are selected from the group consisting of liposomes and micelles.

359. A formulation according to Claim 357 wherein said lipid vesicles comprise a phospholipid.

360. A formulation according to Claim 359 wherein said phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine and phosphatidic acid.

361. A formulation according to Claim 360 wherein said phosphatidylcholine is selected from the group consisting of dioleoylphosphatidylcholine,

dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphatidylcholine.

362. A formulation according to Claim 361 wherein said phosphatidylcholine comprises dipalmitoylphosphatidylcholine.

363. A formulation according to Claim 360 wherein said phosphatidylethanolamine is selected from the group consisting of dipalmitoylphosphatidylethanolamine, dioleoylphosphatidylethanolamine, N-succinyldioleoylphosphatidylethanolamine and 1-hexadecyl-2-palmitoylglycerophosphoethanolamine.

364. A formulation according to Claim 363 wherein said phosphatidylethanolamine comprises dipalmitoylphosphatidylethanolamine.

365. A formulation according to Claim 360 wherein said phosphatidic acid comprises dipalmitoylphosphatidic acid.

366. A formulation according to Claim 357 wherein said lipid vesicles further comprise a polymer.

367. A formulation according to Claim 366 wherein said polymer comprises a hydrophilic polymer.

368. A formulation according to Claim 367 wherein said hydrophilic polymer comprises polyethylene glycol.

369. A formulation according to Claim 357 wherein said fluorinated gas comprises a perfluorocarbon.

370. A formulation according to Claim 369 wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane.

371. A formulation according to Claim 370 wherein said perfluorocarbon gas is selected from the group consisting of perfluoropropane and perfluorobutane.

372. A formulation according to Claim 371 wherein said perfluorocarbon gas comprises perfluorobutane.

373. A formulation according to Claim 357 wherein said gas is derived, at least in part, from a gaseous precursor.

374. A formulation according to Claim 373 wherein said gaseous precursor has a boiling point of greater than about 37°C.

375. A formulation according to Claim 374 wherein said gaseous precursor comprises a perfluorocarbon.

376. A formulation according to Claim 375 wherein said perfluorocarbon is selected from the group consisting of perfluoropentane and perfluorohexane.

377. A formulation according to Claim 357 wherein said receptors comprise the glycoprotein GPIIb/IIIa receptor.

378. A formulation according to Claim 377 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIb/IIIa receptor of no greater than about 10^{-3} molar.

379. A formulation according to Claim 378 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIb/IIIa receptor of less than about 10^{-3} molar.

380. A formulation according to Claim 379 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIb/IIIa receptor of from about 10^{-9} molar to less than about 10^{-3} molar.

381. A formulation according to Claim 380 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIb/IIIa receptor of from about 10^{-7} molar to about 10^{-5} molar.

382. A formulation according to Claim 381 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIb/IIIa receptor of about 10^{-6} molar.

383. A method for the therapeutic delivery *in vivo* of a bioactive agent comprising administering to a patient a therapeutically effective amount of a formulation which comprises, in combination with a bioactive agent, lipid vesicles encapsulating a fluorinated gas, in combination with a targeting ligand, wherein said targeting ligand comprises the sequence Lys-Gln-Ala-Gly-Asp-Val (SEQ ID NO 1), and said fluorinated gas is selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

384. A method according to Claim 383 wherein said lipid vesicles are selected from the group consisting of liposomes and micelles.

385. A method according to Claim 383 wherein said lipid vesicles comprise a phospholipid.

386. A method according to Claim 385 wherein said phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine and phosphatidic acid.

387. A method according to Claim 386 wherein said phosphatidylcholine is selected from the group consisting of dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphatidylcholine.

388. A method according to Claim 387 wherein said phosphatidylcholine comprises dipalmitoylphosphatidylcholine.

389. A method according to Claim 386 wherein said phosphatidylethanolamine is selected from the group consisting of dipalmitoyl-phosphatidylethanolamine, dioleoylphosphatidylethanolamine, N-succinyldioleoyl-phosphatidylethanolamine and 1-hexadecyl-2-palmitoylglycerophosphoethanolamine.

390. A method according to Claim 389 wherein said phosphatidylethanolamine comprises dipalmitoylphosphatidylethanolamine.

391. A method according to Claim 386 wherein said phosphatidic acid comprises dipalmitoylphosphatidic acid.

392. A method according to Claim 383 wherein said lipid vesicles further comprise a polymer.

393. A method according to Claim 392 wherein said polymer comprises a hydrophilic polymer.

394. A method according to Claim 393 wherein said hydrophilic polymer comprises polyethylene glycol.

395. A method according to Claim 383 wherein said fluorinated gas comprises a perfluorocarbon.

396. A method according to Claim 395 wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane.

397. A method according to Claim 396 wherein said perfluorocarbon gas is selected from the group consisting of perfluoropropane and perfluorobutane.

398. A method according to Claim 397 wherein said perfluorocarbon gas comprises perfluorobutane.

399. A method according to Claim 383 wherein said gas is derived, at least in part, from a gaseous precursor.

400. A method according to Claim 399 wherein said gaseous precursor has a boiling point of greater than about 37°C.

401. A method according to Claim 400 wherein said gaseous precursor comprises a perfluorocarbon.

402. A method according to Claim 401 wherein said perfluorocarbon is selected from the group consisting of perfluoropentane and perfluorohexane.

403. A method according to Claim 383 wherein said receptors comprise the glycoprotein GPIIbIIIa receptor.

404. A method according to Claim 403 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIbIIIa receptor of no greater than about 10^{-3} molar.

405. A method according to Claim 404 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIbIIIa receptor of less than about 10^{-3} molar.

406. A method according to Claim 405 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIbIIIa receptor of from about 10^{-9} molar to less than about 10^{-3} molar.

407. A method according to Claim 406 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIbIIIa receptor of from about 10^{-7} molar to about 10^{-5} molar.

408. A method according to Claim 407 wherein said targeting ligand exhibits a binding affinity (K_d) to the GPIIbIIIa receptor of about 10^{-6} molar.

409. A method according to Claim 403 further comprising the administration of a sufficient amount of ultrasound energy to induce rupture of said vesicles.

410. A method according to Claim 409 wherein said glycoprotein GPIIbIIIa receptor is associated with a thrombus.